

Andrews (J. B.)

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By J. B. ANDREWS, A. M., M. D.,

Superintendent of the Buffalo State Asylum for the Insane, Buffalo, N. Y.

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Urethan, or carbamate of ethyl, is one of a class of ethers, derived from carbamic acid. This acid has certain chemical relations with urea, and it is on this account that these ethers have been called urethanes.

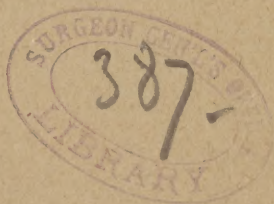
I quote from a translation by Dr. F. R. Campbell, of Buffalo, of an article by Henri Huchard. He gives the formula of urethan as $\text{NH}_2\text{CO}_2\text{C}_2\text{H}_5$. It is found to consist of rhomboidal crystals, fusing at 55° , and distilling at 180° , soluble in alcohol, water and ether.

It was introduced in therapeutics by Schmiedeberg of Strassburg, and has been studied by Jolly and Jacksch of Vienna, by Reigel and Sticker of Giessen, and by Dr. A. L. Myrtle, who gives a record of his experience in the *British Medical Journal*. The first experiments were made upon rabbits and Guinea pigs, in which cases it was pushed to its fullest effects. It was given hypodermically, but produced an irritation similar to that of chloral, "which prevents its being used by this method on the human subject."

I give a brief compend of the observations of experimenters.

Dr. Von Jacksch's investigations were made on twenty cases, with one hundred and ten separate observations. They embraced several varieties of pathological conditions, in many of which other hypnotics were contra-indicated, and urethan rarely failed to produce marked hypnotic effects.

* Read before the Buffalo Medical Club, June 23, 1886.



The *Therapeutic Gazette* in giving a report of its investigation, says:

It seems clear that the principal action of urethan is on the brain, without producing any marked irritation of the peripheral or sensory apparatus—consequently it is useless in the treatment of neuralgic pains, as well as in the pains of locomotor ataxia. But in other conditions, where sleeplessness is the main symptom to be combated, urethan seems to possess the greatest advantages, since it is well borne by the patient; it produces absolutely no unpleasant symptoms, and the sleep which it produces seems identical with normal physiological sleep.

It would also appear that this remedy is particularly suitable for use in the treatment of diseases of children where the need of a safe and sure hypnotic is greatly felt.

The Doctor gave it in doses of from seven and one-half to fifteen grains.

Dr. Huchard, in the translation spoken of, says that he has prescribed urethan in fourteen cases suffering from various degrees of insomnia, and affected with various diseases. With the exception of two cases of tuberculosis with incessant coughing and great dyspnoea, all derived benefit from this drug, which produced calm, peaceful sleep without dreams, digestive disturbance or headache as the sequelæ, and that sleep comes on in from ten minutes to one hour after the administration of the medicine, and lasts from four to ten hours.

The dose which he has given to adults is three or four grams, equal to forty-five and sixty grains. This dose produces better effects than the one and two gram doses directed by most German writers.

Another point Dr. Huchard makes, which I believe to be especially important in cases of insomnia, to produce the best results, is: that the medicine should be given in one large undivided dose. This is much more efficient than giving it in smaller and divided doses.

As a conclusion he states, that he has never seen urethan produce any unpleasant symptoms relating to the stomach, heart or nervous system; hence the remedy may be given with advantage to overcome the restlessness of dyspeptics and those suffering from heart disease, debility and nervous prostration, and that this arises from the fact that urethan is a pure hypnotic and almost destitute of analgesic properties.

Dr. Sticker derives the following conclusions from his investigations as to the action of urethan. This is from the *Therapeutic Gazette* for March, 1886:

Urethan is an excellent cerebral hypnotic, and possesses advantages over the usual hypnotic, in that it is well borne, produces absolutely no unfavorable symptoms, and causes sleep which appears to be perfectly similar to the physiological state.

Urethan appears to be indicated in cases in which the other hypnotics, either on account of their unfavorable action on the heart or respiration, on account of their taste or for some idiosyncrasy of the patient, have to be reduced or stopped.

The minimum dose is fifteen grains, and in persons from fifteen years of age upwards this may be increased to sixty grains without danger.

Dr. A. L. Myrtle reports that since October he has been using urethan in a variety of cases with satisfactory results.

I have used it in over fifty cases as a sedative and hypnotic, and my experience of its action encourages me to recommend it to the readers of the *British Medical Journal*, believing that in certain cases it will prove of great value.

The cases in which I have prescribed it were in the usual run of every-day practice where a sedative or hypnotic was required: general restlessness, sleeplessness, neuralgic catarrh, certain forms of skin affection with great irritation, also rheumatism and gout.

He reports a case as follows:

One gentleman who had suffered from insomnia for weeks, and who can not tolerate opium or chloral took fifteen grains at bed-

time with the most perfect results. He wrote to me stating: "The sleep caused was the most pleasant and refreshing. I woke without a headache, with appetite for breakfast, and what was equally agreeable, there was no interruption of any of my functions."

He sums up his experience; that the remedy is decidedly calmative and agreeable, causing no unpleasant effects, such as nausea, flatulence, constipation or headache. It does not affect the nerve centres, circulation or respiration, but spends itself upon the cerebrum. He then states that the only objection to it is its price.

These are all the experiments with the drug that have fallen under my eye. I determined to make some personal investigation, and after considerable trouble succeeded in obtaining a small quantity of the drug. This is manufactured by Merck, and put up in ounce bottles at a cost at first of \$2.25 per ounce, now reduced to \$1.65.

The first experiment was made on the 8th of May, when I took thirty grains of urethan at three p. m. Before taking it, the pulse stood at eighty; in fifteen minutes it had fallen to seventy; and at forty minutes was substantially the same. I fell asleep while sitting in my chair about half an hour after taking the medicine. The sleep was natural without any unpleasant sensations, without disturbance of respiration or the pupils of the eye. It was not prolonged, but was interrupted by the taking of the sphygmographic trace. After this interruption no further opportunity was given for sleep, as I got up and walked about.

On May 14, a second experiment was made. I took fifty grains of urethan at 8.25 p. m. The pulse before taking stood at eighty-eight, in fifteen minutes the pulse was reduced to eighty-two, and in an hour after

taking to eighty. At nine o'clock, thirty-five minutes after taking the drug, I fell asleep. At 9.20 tracing was taken; at 9.35 I was awakened by a report from the night-watch regarding patients which demanded my attention. This aroused me so fully that I did not sleep again. The character of the sleep and the effects of the drug were the same as before reported.

On May 27th the third experiment was made. I took sixty grains of urethan at ten minutes past nine P. M.; pulse before taking stood at eighty-six, in ten minutes had fallen to eighty-four; in forty minutes to seventy-two, and in fifty minutes to seventy. A tracing was taken ten minutes after taking the medicine, another forty minutes after, and another fifty minutes after. At 9.35, twenty minutes after taking the medicine, I was asleep. At 9.45 sleep was profound, respiration seventeen. At 10 P. M., I still slept, respiration sixteen; after this I was awakened, and though feeling profoundly sleepy I did not yield further to the sensation. Retired at 11 o'clock, and slept soundly as usual all night.

In all of these experiments the sleep seemed to be of a strictly physiological character. Its approach was normal, and on awaking there was no headache nor any feeling other than that of having been aroused from pleasant sleep. There was no subsequent disturbance of the stomach of any kind, and, in fact, nothing to distinguish it from a pleasant period of repose.

The drug was taken simply dissolved in water and no attempt made to cover it. The taste is not unpleasant, resembling in a mild degree that of spirits of nitre.

For administration, it can be readily covered by any of the ordinary excipients. In regard to the tracings taken, I was unable to make out any marked effect upon the character of the pulse, except a reduction in the number of the beats, hence these are not presented.

I have prescribed the remedy in more than twenty cases in doses from seven to sixty grains, and give a record of a portion of these.

The first dose of seven grains was given to a man, case of dementia, and as might have been expected, produced no appreciable results.

Second case, a woman, chronic mania, who is frequently noisy and out of bed for hours at a time, took twenty grains and slept all night. This was followed by four nights of quiet rest, without medicine, then followed a night of unrest, after which, under a repetition of the dose, she slept well.

Third case, woman, chronic mania, who had the previous night been noisy and out of bed for hours, received a dose of twenty grains, and slept all night.

Fourth case, woman, with acute mania, was awake, out of bed and noisy the whole night previous to taking it; was given thirty grains and slept well; the following night she received nothing and slept well; the next night, however, she was awake for several hours. The following night was given thirty grains, and slept well.

Fifth case, a woman, chronic melancholia, was awake all the previous night, slept well under thirty grains of urethan.

Sixth case, woman, with dementia, had been awake and out of bed all night prior to taking the medicine, slept well under twenty grains.

Seventh case, woman, acute mania, was awake the whole of the previous night, slept well under a twenty grain dose. The second night thereafter was wakeful, but slept well the following night upon another dose of twenty grains.

Eighth case, woman, with chronic melancholia, was awake all night previous to taking the medicine, but slept well under thirty grains.

Ninth case, woman, with general paresis, awake all night previous, slept well under thirty grains.

Tenth case, woman, acute mania, violently excited, noisy, awake all the night previous, slept well under thirty grains.

Eleventh case, man, with acute melancholia, who had been restless and sleepless, slept well under thirty grains.

Twelfth case, man, with general paresis, who had been violently disturbed, slept well under fifteen grains. This soon lost its effect, but it was regained under the use of a dose of thirty grains. After a short period, he became disturbed and sleepless again, and was given doses of forty, fifty and sixty grains, which controlled him a part of the time; some nights, however, it seemed to have very little effect.

Thirteenth case, man, with general paresis, who had been noisy and disturbed, slept well under twenty-five grains, and in one instance slept all night under the use of twenty grains.

Fourteenth case, man, with acute violent mania, received the first night after admission, bromide of potash and chloral hydrate, each twenty grains. The first night slept well; the second night was awake and out of bed three hours; third night was given forty grains of urethan, slept all night; fourth night the same, with the same result; fifth night no medicine was given, awake until two o'clock. In this case it has since been carried up to sixty grains with good results.

Fifteenth case, man, with melancholia, had steadily improved, and had reached a very comfortable condition when he became restless and sleepless at night. The state seemed to be one of simple insomnia. He was given fifteen grains, which was continued for one week, giving good refreshing sleep and breaking up the previous sleepless condition.

Sixteenth case, a man, with acute mania. The night before taking the urethan, was awake and noisy most of the night. Was given fifty grains and slept well. On the second night he was given the same dose at ten o'clock and slept all night, after twelve. The third night under the same dose slept all night; the fourth night all night, also the fifth, sixth and seventh nights. Medicine discontinued and patient was awake from one o'clock, and the following night from three o'clock on.

Seventeenth case, man with paresis, who was noisy, sleepless and out of bed pounding on the door prior to taking the urethan, the following night was given fifty grains, and slept all night. Under the same dose the second night he was disturbed for one hour. Upon the third night slept all night. The fourth night was awake from twelve until morning. Fifth night slept all night; sixth night same; seventh, medicine was discontinued. He was noisy and disturbed most of the night. From this time his sleep was somewhat broken, though better than before the medicine was given.

Eighteenth case, man, with acute mania, who had been persistently noisy and awake several hours every night for weeks together, was given thirty grains of urethan and slept all night. The following night he was given forty grains, and slept well until three o'clock, after which he was noisy. The following night no medicine was given, and he was noisy and out of bed from one o'clock.

On analyzing the cases we find that there were nine of women and nine of men. Divided as to forms of insanity, acute mania, 6; paresis, 4; melancholia, 4; chronic mania, 2; dementia, 2.

The dose most commonly given was thirty grains. In two instances, however, it was carried to the extent

of sixty grains. This was ventured upon after my personal experience with the same dose.

So far the results have been quite favorable, and show that urethan has marked hypnotic power. There were in no case any unpleasant results of any kind. There is nothing to indicate any further action than upon the cerebrum. The effects of the drug were felt, so far as we were able to judge, within an hour after its administration, and the sleep lasted in most cases from the time of observation, commencing at ten o'clock, until five o'clock in the morning.

We do not consider these experiments sufficient to enable us to speak positively of the effect of the drug, or to give it its true position as a sleep producing agent. This can be done only after it has been used a long time and in large quantities. They are, however, such as to lead us to recommend its trial in cases where other drugs are contra-indicated, either from the pathological state present, the unpleasantness of the dose, or the peculiar idiosyncrasy of the patient.

It may do well in private practice, where there is such a demand for a variety of hypnotic drugs, and I would commend it to you for careful consideration and further use.

We have used in all something over five ounces of urethan. This upon an average of thirty grains to a dose, which is probably very nearly correct, would give eighty doses as having been administered.

Equally good results followed in cases which have not been reported as in those which are referred to in this paper.

NOTE.—Since this paper was read, one or more observers have recorded nausea as a symptom following the administration of large doses of urethan. In the discussion which followed the reading of the paper before the Club, Professor Stockton, of Buffalo, reported a case of nausea and vomiting produced by full doses of the drug.

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